REMARKS

I. The Amendment

The term "about" has been deleted from claim 1. Claim 1 has also been amended to specify that the overexpression of AAV Rep 52 and Rep 40 proteins in the claimed cell is in comparison the the expression of the proteins when under the control of the AAV p19 promoter. Specification support for this amendment appears, for example, as described in Section II of Applicants' response of October 4, 2006. Claims 3 and 10 have been amended to specify that AAV helper functions are provided in the claimed methods by infecting a cell with helper virus of AAV or by expressing helper virus proteins in a cell. Specification support for this amendment appears, for example, at page 5, lines 19-24. Finally, claim 9 has been amended to indicate that the rAd used in the methods retains the ability to insert an expression construct encoding AAV Rep 52 and Rep 40 proteins into a cell. This function is what is required by original claim 4. The amendments do not introduce new matter.

II. The Rejections under 35 U.S.C. § 112, Second Paragraph Should be Withdrawn

Claims 1, 2, 9, 10-14 and 21-38 are rejected under 35 U.S.C. § 112, second paragraph for purportedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. In particular, the Examiner maintained his assertion that the term "overexpresses AAV Rep 52 and Rep 40" in claim 1 is unclear. In addition, the Examiner maintained the rejection of claim 9 because the recitation of "derived from simian Ad SV-20" is indefinite.

As explained in previous responses, the term "overexpresses AAV Rep 52 and Rep 40" in claim 1 would be understood by a person skilled in the art to mean that the cell expresses greater levels of Rep52 and Rep40 proteins than the levels obtained from the wild type native p19 promoter alone. Claim 1 has been amended to include a limitation to that effect.

Similarly, with respect to the term "derived from simian Ad SV-20" in claim 9, a person skilled in the art would know what viral elements are necessary for a functional recombinant adenovirus vector and would know how to make a functional recombinant

adenovirus vector. Claim 9 has been amended to specify that the rAd retains the ability to introduce the expression cassette encoding AAV Rep 52 and Rep 40 proteins into the claimed cell.

In view of the foregoing amendments and remarks, the rejections under 35 U.S.C. § 112, second paragraph should be withdrawn.

III. The Rejections under 35 U.S.C. § 112, First Paragraph Should be Withdrawn

Claims 3-14, 21-29 and 31-38 remain rejected under 35 U.S.C. § 112, first paragraph because the specification assertedly does not enable methods of producing rAAV or rAAV-producing cells by "introducing" AAV helper virus proteins into a cell. The Examiner indicated that transforming or transfecting nucleic acids encoding the proteins into cells was enable. Claims 3 and 10 have therefore been amended to recite that AAV helper functions are provided by infecting a cell with helper virus of AAV or by expressing helper virus proteins in the cell

The rejections under 35 U.S.C. § 112, first paragraph should thus be withdrawn.

IV. The Rejections under 35 U.S.C. § 102(b) Should Be Withdrawn.

The Examiner maintained the rejection of claims 1-3, 10-13, 21, 23, 24, 30, 32 and 36 under 35 U.S.C. § 102(b) as being anticipated by Natsoulis *et al.* (U.S. Patent No. 6,027,931) or Xiao *et al.* (*J. Virol.* 72(3): 2224-2232, 1998).

The Examiner first indicated the rejections were maintained because the claims embrace a "wide range" of Rep78/68 expression levels because claim 1 recites the proteins are expressed at "about" the level of expression when under the control of the p5 promoter.

While Applicants continue to dispute that either Natsoulis *et al.* or Xiao *et al.* describe host cells in which Rep 78 and Rep 68 proteins are expressed at "about" the levels of expression when under the control of the p5 promoter, Claim 1 has been further amended to delete the "about" term objected to by the Examiner.

The rejection of claim 1 (and claims dependent thereon) under 35 U.S.C. §102(b) should therefore be withdrawn.

The Examiner also indicated the rejection of claims 3 and 10 was maintained based on the argument that Natsoulis *et al.* taught the addition of Rep/Cap expression constructs sequentially to cells. The Examiner pointed to the Office Action mailed 7/29/2005 that indicated support for his argument was found in Natsoulis *et al.* at column 12, lines 39-42 and in Example 1.

In fact, neither Example 1 nor column 12 of the cited document describe a method according to the present claims. As previously noted, present claim 3 requires that an expression cassette encoding Rep 52 and Rep 40 proteins be introduced into a cell already comprising a rAAV genome, AAV rep-cap proteins and AAV helper functions. Likewise, claim 10 requires that supplemental Rep 52 and Rep 40 proteins be introduced into a cell already comprising a rAAV genome and AAV rep-cap proteins. Example 1 of Natsoulis *et al.* involves **one** transfection of 10 micrograms of **one** of six different rep-cap protein-encoding constructs. There is no second introduction of rep-cap sequences or proteins described in Example 1. Each 293 cell line is transfected only once with one rep-cap construct. See Natsoulis *et al.* Example 1 as well as the data presented in Table 1.

Natsoulis *et al.* column 12, lines 39-42 states that an AAV vector and AAV helper function vector can be sequentially transfected into a host cell. Regarding how the two vectors are supposed to work with respect to each other, column 7, lines 1-12 of Natsoulis *et al.* states that AAV helper functions include the rep and cap regions and are used to complement AAV functions that are missing from AAV vectors. Assuming that is the case, then the sequential transfection of column 12 is not a sequential transfection of rep-cap sequences.

Therefore, neither independent claims 3 and 10 nor claims dependent thereon are expressly or inherently anticipated by Natsoulis *et al.*. and the rejection of those claims under U.S.C. §102(b) should be withdrawn.

V. The Rejection under 35 U.S.C. § 103(a) Should Be Withdrawn

The Examiner maintained the rejection of claims 22, 26, 28 , 29 31, 35, 37 and 38 under 35 U.S.C. § 103(a) as being unpatentable over Natsoulis *et a.* (U.S. Patent No. 6,027,931) in view of Hardy (U.S. Patent No. 6,429,001). The Examiner stated that Hardy teaches that AAV host cells include the claimed cell types: HeLa, WI-38, MRC-5 and Vero. Similarly, claims 25 and 34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Natsoulis *et al.* in view of Murphy (U.S. Patent No. 6,635,476). The Examiner stated that Murphy teaches that the PERC.6 cells line is useful for producing adenovirus and rAAV. Claims 27-29 and 36-38 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Natsoulis *et al.* in view of Potash *et al.* (U.S. Patent No. 5,911,998). The Examiner stated that Potash *et al.* teaches that the MRC-5, WI-38 and FRhL-2 cell lines may be used for vaccine production.

As the primary document, Natsoulis *et al.*, cited in the rejection does not teach or suggest methods according to the claims (see Section IV above), combinations of it with other documents that similarly do not teach or suggest methods as claimed do not render the claims obvious. Therefore, the rejections under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants believe pending claims 1-3-10, 12-14, 18, 19 and 21-38 are in condition for allowance and early notice thereof is requested. If further discussion would expedite allowance of the claims, the undersigned can be contacted at the telephone number below.

Respectfully submitted,

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